



# Effects of management practices, animal transport and barn climate on animal health and antimicrobial use in Swiss veal calf operations

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## ABSTRACT

To assess the effects of transport, management factors and barn climate on calf health, 43 Swiss veal farms (11 large farms fattening  $\geq 100$  calves and 32 small farms fattening  $> 20$  but  $< 100$  calves per year) were monitored in a prospective cohort study over a period of one year. Detailed questionnaires on farm structure, management, housing system and animal health were filled out with the farmers during bimonthly visits, and barn temperature, humidity, ammonia and  $\text{CO}_2$  concentrations were measured. Temperature and humidity were also measured continuously over 72 h once each in winter and summer. In addition, calf purchase and transport from birth farm to fattening unit were documented by the farmers, and the study team accompanied one transport per farm whenever possible. Antimicrobial treatment incidence was calculated from the used daily dose ( $\text{TI}_{\text{UDD}}$ ). Risk factors for mortality, average daily weight gain (ADG) and antimicrobial use, as well as factors related to transport and barn climate measures were evaluated with mixed regression models.

The overall mortality rate was 5.1% (6.2% in large herds and 3.1% in small ones). Identified risk factors for mortality  $> 3\%$  included a lower number of calves fattened per year and a good hygiene of the feeder. This surprising result was likely due to the fact that the threshold of 3% mortality was rather exceeded in smaller farms. Furthermore, higher temperature variation (range between maximal and minimal temperature over 3 measurement days) in the calf pen was associated with mortality  $> 3\%$  in the univariable analysis.

The overall mean ADG was  $1.40 \pm 0.16$  kg. Calf purchase was significantly associated with decreased ADG.

The median overall  $\text{TI}_{\text{UDD}}$  was eight daily doses per calf and year (2.1 in small farms and 26 in large farms, respectively); the main indication for treatment was respiratory disease (81.1%). Risk factors for increased TI were no quarantine upon arrival, access to an outside pen, higher numbers of calves per drinking nipple, mechanical ventilation, vaccination against bovine respiratory disease, and a maximum ammonia value  $> 10$  ppm in the calf pen. In addition, a higher number of birth farms and calf purchase from markets were associated with increased TI in the univariable analysis.

The identified risk factors associated with increased TI and mortality and with decreased ADG should be addressed in priority in veal calf operations to improve calf health and reduce antimicrobial use.

## 1. Introduction

Concerns about increasing isolation rates of bacteria resistant to one or several antimicrobial drugs in Europe and globally have led to recognition of the need for measures to control the further spread of resistances (WHO, 2014, 2018; ECDC, 2015). Non-human use of antimicrobials has been linked to an increased risk of human exposure to resistant bacteria and treatment failure (WHO, 2017). A total of 32.3 tons of active substance of antimicrobials was marketed for animals in Switzerland in 2017. Its main part was administered orally (65%), mainly in form of premixes (80%; BLV, 2017). The largest

amount of antimicrobials used in the veal calf industry is administered orally in form of group treatments (Lava et al., 2016b), mostly for metaphylactic purposes (Sargeant et al., 1994a; Pardon et al., 2012a; Catry et al., 2016). Metaphylactic use of antimicrobials is defined as the simultaneous treatment of clinically healthy and diseased animals in the same pen or group. Prophylactic use is defined as the treatment of healthy animals to prevent diseases (Aarestrup, 2005). In Switzerland, metaphylactic and prophylactic use of antimicrobials is allowed, but it is not allowed to dispense antimicrobials for (future) prophylactic treatments beyond what will be used for the current indication (Verordnung über die Tierarzneimittel, 2004).

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The main indications for antibiotic treatment in individual calves are bovine respiratory disease (BRD), digestive disorders, otitis and lameness (Menéndez González et al., 2010; Luginbühl et al., 2012; Fertner et al., 2016; Lava et al., 2016b). Individual treatments of veal calves have been reported to involve critically important antimicrobials in almost 75% of the cases in commercial operations and 56% in operations with improved welfare standards (Beer et al., 2015; Lava et al., 2016b). In the Netherlands, the treatment incidence (TI) for veal calves was 34 daily doses per calf and year in 2008, which has decreased to approximately 20 daily doses per calf and year in 2017 (MARAN, 2008, 2017). A previous study in Switzerland has shown similar figures (21 daily doses per calf and year; Lava et al., 2016b). These figures confirm that antimicrobial use in veal calves is problematic in Switzerland and other European countries.

Mortality is an important economic parameter in the veal calf industry (Bleul, 2011; Pardon et al., 2013). It has been estimated to 3%–5% in Switzerland (Busato et al., 1997; Bähler et al., 2012; Luginbühl et al., 2012; Lava et al., 2016b), and between 3.5% and 7.6% in other countries (Gulliksen et al., 2009b; Vaarst and Sørensen, 2009; Pardon et al., 2012b; Windeyer et al., 2014; Winder et al., 2016; Renaud et al., 2017). A significant association has been demonstrated between mortality and TI (Bähler et al., 2012; Jarrige et al., 2017).

Factors that can influence calf health and, consequently, mortality and TI are numerous. Calf diseases have been shown to be more frequent in winter and in higher mountain zones (Busato et al., 1997). Furthermore, the possibility to nest, lower air temperature in the calf pen and increased barn volume have been associated with less BRD, whereas larger numbers of calves per pen, increasing age difference among calves of the same group, calf purchase, mechanical barn ventilation and exposure to noxious gases have been associated with increased risk of BRD (Svensson et al., 2003; Lago et al., 2006; Gulliksen et al., 2009a; Snowden, 2009; Brscic et al., 2012; Woolums et al., 2013).

Regarding risk factors for increased calf mortality, the following parameters have been identified as significantly associated: calf purchase, access to outside pens, increased herd and group size, birth during winter, passage(s) through a market, extreme temperatures and dairy breed (Martin et al., 1975; Waltner-Toews et al., 1986; Svensson et al., 2006; Gulliksen et al., 2009b; Bleul, 2011; Pardon et al., 2012b; Lava et al., 2016a; Murray et al., 2016; Renaud et al., 2017).

Although the assumption that TI is a reliable indicator of disease incidence must be questioned, especially in veal calves which are often treated pro- or metaphylactically at entry in the fattening unit, these two factors are generally considered to be related (Sargeant et al., 1994a, 1994b; Pardon et al., 2012b). It has been shown that farmers fattening only their own calves have a lower antimicrobial consumption than farmers who purchase additional calves (Luginbühl et al., 2012; Lava et al., 2016a). In addition, larger herd size was associated with increased antimicrobial consumption, as metaphylactic treatment upon arrival is applied more often in those herds (Lava et al., 2016a). These observations suggest that management factors may have a larger effect on antimicrobial use than calf health itself, thus the relationship between calf health and antimicrobial use remains unclear.

It is well established that sick and treated calves have lower average daily weight gains (ADG) compared to healthy and untreated calves (Bateman et al., 1990; Virtala et al., 1996; Svensson and Liberg, 2006; Thompson et al., 2006), thus ADG can serve as an indicator of calf health.

Veal calves in Switzerland usually enter the fattening unit around the age of three weeks and are fattened until a maximum carcass weight of 160 kg (Eidgenössische Zollverwaltung, 2016). They are normally fed with whole milk or milk by-products supplemented with powder (Bähler et al., 2012). Welfare regulations prescribe that calves must be kept in groups in loose housing stalls and have ad libitum access to water and roughage (Tierschutzverordnung, 2008).

Risk factors potentially associated with calf health, treatment intensity and mortality have not been evaluated prospectively in Swiss

veal calves to date. Therefore, the aim of the present study was to identify risk factors for increased antimicrobial drug use and mortality as well as for decreased ADG in Swiss veal calf operations, with emphasis on calf transport from birth farm to veal fattening unit and on barn climate parameters. Based on the results, recommendations for the improvement of management practices and housing conditions should be developed, which eventually should result in better calf health and reduced antimicrobial use.

## 2. Materials and methods

### 2.1. Study design and farm selection

The target population of this prospective cohort study consisted of all fattening units in Switzerland with at least 25 fattened calves per year and operating all year round. The farmers were informed about the project through the Swiss veal farmers association (Schweizer Kälbermästerverband) and various agricultural magazines and newspapers in the German and French speaking areas of Switzerland. Interested farmers could contact the Clinic for Ruminants in Bern. Whether a farm met the criteria for participation in the project was assessed during an initial phone conversation. If so, an appointment for a first farm visit was arranged. The farms were divided into two groups at the beginning of the project: large farms fattening  $\geq 100$  calves per year and small farms fattening  $\geq 25$  but  $< 100$  calves per year. However, the effective number of fattened calves was not known until the last visit at the end of the project. Four participating farms eventually had less than 25 fattened calves per year (21, 22, 22 and 23 respectively), which would have been an exclusion criteria by definition at the start of the project. The data of these farms were nonetheless used in the analyses as all data had been acquired by the time the definitive number of calves was known and no farm had fattened less than 21 calves. All analyses were performed with the farms assigned correctly according to the effective number of calves fattened during the study period. Recruitment started in June 2016, inclusion in the study was possible until September 2016. By then, 43 farms had been recruited. This sample size was sufficient to detect a decrease of  $TI_{\text{UDD}}$  of 13 for a given risk factor, assuming a mean of  $TI_{\text{UDD}}$  of 21 in the group without the protective factor, a variance of 225 (Lava et al., 2016b), a confidence level of 95% and a power of 80%. Sample size was calculated with EpiTools (<http://epitools.ausvet.com.au>).

### 2.2. Farm visits, questionnaires, treatment records and measurements

Each farm was observed for a one-year period between July 2016 and November 2017. During this period, the farms were visited six times, all-in-all-out farms at the beginning and end of each fattening period and farms with continuous arrival of calves every 2–3 months. One all-in-all-out farm was visited only four times because the fattening period was longer with a break of two months between the two fattening groups. Another farm was visited eight times, because the fattening periods were very short.

During the first farm visit, a questionnaire adapted from Lava et al. (2016a) was filled out with the farmers. The questionnaire had been tested with 3 farmers and 3 veterinarians prior to the study. It consisted of questions covering the following issues: farm location and personal working on the farm, number of fattened calves per year and other animals on the farm, housing, ventilation, cleaning of the barns, purchase and transport as well as feeding and vaccinations of calves, antimicrobial use, health information on the calves, number of deaths and unwanted early slaughter (Table 1). Each farmer received an especially designed booklet to register antimicrobial treatments containing detailed information about illness duration and treatment results in addition to the standard treatment journal prescribed by Swiss law that contains data about the date, number and identification of treated calves, reason for treatment, name and dosage of the drug, application

**Table 1**Farm characteristics and treatment incidence (TI<sub>UDD</sub> and TI<sub>DDD</sub>) in 43 Swiss veal calf operations in 2016/2017.

Parameter	Category	Number of farms	Percent		
Farm size <sup>a</sup>	Large farms	11	26%		
	Small farms	32	74%		
Agricultural zone	Midland zone	13	30%		
	Hill zone	6	14%		
	Mountain zone	24	56%		
Purchase	Yes	34	79%		
	No	9	21%		
Access to outside pen	Yes	25	58%		
	No	18	42%		
Examination at arrival	Yes	6	14%		
	No	28	65%		
	N/A <sup>b</sup>	9	21%		
Metaphylactic treatment upon arrival	Yes	11	26%		
	No	32	74%		
Vaccination against BRD <sup>c</sup>	Yes	14	33%		
	Partially <sup>d</sup>	7	16%		
	No	22	51%		

  

Parameter	Category	Median	Quartile		Range
			25th	75th	
Number of fattened calves per year	Overall	54	39.0	102.0	21-667
	Small farms	49	34.8	60.8	21-89
	Large farms	164	118.0	248.0	102-667
Group size <sup>e</sup>	Overall	10	6.7	18.3	3-50
	Small farms	8	6.2	11.8	3-28
	Large farms	23	20.5	37.6	11-50
Overall area (m <sup>2</sup> ) per calf <sup>f</sup>		3	2.4	4.2	1.3-10.9
Bedded area (m <sup>2</sup> ) per calf <sup>f</sup>		3	2.1	3.5	1.3-10.9
Average temperature in calf pens (°C) <sup>g</sup>		16	11.3	21.3	− 2.2-32.8
Maximum temperature variation (°C) <sup>h</sup>		10	7.8	13.2	3.6-31.4
Average humidity in calf pens (%) <sup>g</sup>		62	56.0	66.8	39.0-79.0
Maximum variation of humidity (%) <sup>h</sup>		36	28.0	45.3	15-69
Maximum carbon dioxide in calf pens (ppm) <sup>g</sup>	Overall	865	627.8	1140.8	182-2550
	Small farms	789	621	1038	182-2131
	Large farms	1117	858	1394	480-2550
Maximum ammonia in calf pens (ppm) <sup>g</sup>	Overall	0	0	7.0	0-25
	Small farms	0	0	7.0	0-25
	Large farms	6	0	8.8	0-22
Average number of birth farms per 10 calves	Overall	4	1.1	6.3	0.6-9.7
	Small farms	2	1.0	5.8	1-9.7
	Large farms	6	4.1	8.1	0.6-8.9
Transport distance (km)	Overall	16	1.8	30.5	0-250
	Small farms	11	0	23.7	0-128
	Large farms	39	18.7	77.9	18-250
Treatment incidence (TI <sub>UDD</sub> ) in used daily doses per calf per year	Overall	8	3.3	14.7	0-50.2
	Small farms	5	2.1	9.6	0-34.7
	Large farms	26	14.7	34.4	5.8-50.2
Treatment incidence (TI <sub>DDD</sub> ) in defined daily doses per calf per year	Overall	9	4.4	16.9	0-40.6
	Small farms	7	2.4	12.2	0-35.4
	Large farms	18	13.6	31.6	6.9-40.6

<sup>a</sup> Large farms ≥ 100 calves fattened per year, small farms > 20 but < 100 calves fattened per year.<sup>b</sup> N/A: not applicable (no calf purchase).<sup>c</sup> BRD: bovine respiratory disease, vaccination with a modified live viral vaccine.<sup>d</sup> Partially: not all year around, for example only in winter.<sup>e</sup> Group size: average number of calves per pen.<sup>f</sup> Without outside pen.<sup>g</sup> Measured punctually during each farm visit.<sup>h</sup> Measured continuously over 72 h.

**Table 2**  
Univariable mixed logistic model of potential risk factors for mortality > 3% in Swiss veal herds.

Parameter	Category	n <sup>i</sup>	≤ 3%	> 3%	Wald p-value
Agricultural zone <sup>i</sup>	Midland zone	13	68.3	31.7	0.8
	Hill zone	6	63.3	36.7	
	Mountain zone	24	70.0	30.0	
Stocking method <sup>*,j</sup>	All-in all-out	12	59.3	40.7	0.07
	Continuous	31	72.1	27.9	
Access to outside pen <sup>i</sup>	Yes	25	69.8	30.2	0.6
	No	18	66.7	33.3	
Ventilation <sup>*,k</sup>	Natural	88	73.9	26.1	0.16
	Mechanical	125	64.8	35.2	
Shared airspace <sup>h,l</sup>	Yes	24	66.1	33.9	0.39
	No	19	71.6	28.4	
Hay or straw storage near calf pen(s) <sup>i</sup>	Yes	5	65.2	34.8	0.7
	No	38	69.0	31.0	
Pen change during fattening period <sup>i</sup>	Yes	22	67.0	33.0	0.6
	No	21	70.2	29.8	
Disinfection of calf pens <sup>i</sup>	≥ 3x per year	9	66.7	33.3	0.4
	< 3x per year	5	80.0	20.0	
	Never	29	67.1	32.9	
Duration of sanitary break between groups <sup>*,j</sup>	≥ 1 week	8	77.5	22.5	0.14
	< 1 week	7	55.9	44.1	
	None	28	69.1	30.9	
Cleaning of automatic feeder <sup>i</sup>	Daily	33	71.2	28.8	0.25
	Less than daily	9	62.2	37.8	
Hygiene of the feeder <sup>*,k</sup>	Good	126	77.8	22.2	< 0.001
	Not good	81	55.6	44.4	
Calves per drinking nipple <sup>*,k</sup>	1-5	29	69.0	31.0	0.008
	6-10	96	78.1	21.9	
	> 10	80	56.3	43.7	
Vaccination against BRD <sup>c,k</sup>	Yes	82	65.9	34.1	0.5
	No	131	70.2	29.8	
Purchase <sup>*,j</sup>	Yes	34	65.1	34.9	0.03
	No	9	81.8	18.2	
Examination at arrival <sup>*,j</sup>	Yes	6	75.9	24.1	0.03
	No	28	62.9	37.1	
	N/A <sup>b</sup>	9	81.8	18.2	
Quarantine upon arrival <sup>*,j</sup>	Yes	8	76.9	23.1	0.02
	No	26	61.5	38.5	
	N/A <sup>b</sup>	9	81.8	18.2	
Metaphylactic treatment upon arrival <sup>*,k</sup>	Yes	53	49.1	50.9	< 0.001
	No	160	75.0	25.0	
Passage(s) through markets <sup>i</sup>	Yes	18	60.7	39.3	0.07
	No	24	73.1	26.9	
Maximum ammonia concentration (ppm) <sup>k,m</sup>	≤ 10	185	69.2	30.8	0.6
	> 10	25	64.0	36.0	

The distribution of the factors is shown in % of herds.

\* Factors tested in the multivariable model ( $p < 0.2$ ).

<sup>b</sup> N/A: not applicable (no calf purchase).

<sup>c</sup> BRD: bovine respiratory disease, vaccination with a modified live viral vaccine.

<sup>i</sup> The total number of observations is not always the same because varying observations were recorded in every season and constant factors were recorded only at the beginning of the project.

<sup>j</sup> Parameters measured/assessed once (overall).

<sup>k</sup> Parameters measured/assessed seasonally.

<sup>l</sup> Shared airspace with any cattle other than fattening calves.

<sup>m</sup> In the calf pens per season.

route, treatment duration and withdrawal period.

In addition to the questionnaire, the farm visit consisted of a detailed documentation of the housing system, including measurements of the building(s)' and calf pens' size, assessment of the structure of calf pens, bedding, group size and composition, hygiene (assessed subjectively) as well as supply of milk, roughage and water. In addition,

measurements of temperature, humidity, and concentrations of carbon dioxide (Handheld Indoor Air Quality CO<sub>2</sub>-Meter Model CO240, Extech Instruments, Distrelec AG, 8606 Nanikon, Switzerland) and ammonia (Eingasmessgerät Dräger Pac 7000- Ammoniak, Dräger AG, 3097 Liebfeld, Switzerland) were performed at five different locations in the calf pens. Based on these five measurements, the mean temperature and

**Table 3**

Univariable mixed linear model of associations between potential risk factors and average daily weight gain in kg in Swiss veal herds.

Parameter	Category	<i>n</i> <sup>i</sup>	Mean	Standard deviation	Wald <i>p</i> -value
Agricultural zone <sup>*,j</sup>	Midland zone	13	1.49	0.21	< 0.001
	Hill zone	6	1.39	0.07	
	Mountain zone	23	1.35	0.13	
Stocking method <sup>*,j</sup>	All-in all-out	11	1.37	0.07	0.13
	Continuous	31	1.41	0.19	
Access to outside pen <sup>l</sup>	Yes	24	1.40	0.16	0.7
	No	18	1.40	0.18	
Ventilation <sup>k</sup>	Natural	78	1.43	0.26	0.4
	Mechanical	104	1.39	0.17	
Shared airspace <sup>*,j,l</sup>	Yes	24	1.41	0.19	0.16
	No	18	1.38	0.11	
Hay or straw storage near calf pen(s) <sup>j</sup>	Yes	5	1.34	0.20	0.3
	No	37	1.41	0.16	
Pen change during fattening period <sup>l</sup>	Yes	22	1.36	0.15	0.2
	No	21	1.44	0.17	
Disinfection of calf pens <sup>l</sup>	≥ 3x per year	9	1.36	0.08	0.5
	< 3x per year	5	1.40	0.08	
	Never	28	1.41	0.19	
Hygiene of the feeder <sup>*,k</sup>	Good	108	1.45	0.19	< 0.001
	Not good	69	1.34	0.23	
Feeding frequency <sup>*,j</sup>	Ad libitum	36	1.40	0.17	0.16
	Restricted	6	1.45	0.13	
Roughage <sup>*,k</sup>	Yes	114	1.43	0.19	0.01
	No	68	1.37	0.24	
Vaccination against BRD <sup>c,k</sup>	Yes	67	1.40	0.18	0.9
	No	115	1.40	0.23	
Purchase <sup>*,j</sup>	Yes	33	1.35	0.12	< 0.001
	No	9	1.58	0.19	
Passage(s) through markets <sup>i</sup>	Yes	17	1.37	0.08	0.2
	No	24	1.43	0.20	
Examination at arrival <sup>*,j</sup>	Yes	5	1.67	0.08	< 0.001
	No	28	1.35	0.12	
	N/A <sup>b</sup>	9	1.58	0.19	
Quarantine upon arrival <sup>*,j</sup>	Yes	8	1.37	0.11	< 0.001
	No	25	1.34	0.12	
	N/A <sup>b</sup>	9	1.58	0.19	
Metaphylactic treatment upon arrival <sup>k</sup>	Yes	40	1.37	0.16	0.5
	No	142	1.41	0.22	
Maximum ammonia value (ppm) <sup>k,m</sup>	≤ 10	158	1.40	0.21	0.7
	> 10	22	1.40	0.19	

\* Factors tested in the multivariable model ( $p < 0.2$ ).<sup>b</sup> N/A: not applicable (no calf purchase).<sup>c</sup> BRD: bovine respiratory disease, vaccination with a modified live viral vaccine.<sup>i</sup> The total number of observations is not always the same because varying observations were recorded in every season and constant factors were recorded only at the beginning of the project.<sup>j</sup> Parameters measured/assessed once (overall).<sup>k</sup> Parameters measured/assessed seasonally.<sup>l</sup> Shared airspace with any cattle other than fattening calves.<sup>m</sup> In the calf pens per season.

humidity and the maximum concentration of carbon dioxide and ammonia were recorded for every visit.

During each consecutive farm visit, a shorter questionnaire was filled out with the farmers to register any management changes. The measurements of climate parameters were repeated at each visit and the number of calves and their distribution in different pens was registered. Furthermore, treatment records, slaughter data and transport forms were collected.

At the end of the project, effective vaccinations, numbers of dead calves and unwanted early slaughter in the past year were recorded for each farm.

In addition to the repeated punctual measurements performed during farm visits, temperature and humidity in the calf pens were recorded with two data-loggers (Testo 174H Mini-Datenlogger, Testo AG, 8617 Mönchaltorf; one measurement every 15 min) during 72 consecutive hours, once in summer (June to August) and once during winter (December to February). Based on these measurements, maximum variations of temperature and humidity over 72 h were calculated separately for summer and winter, by subtracting the lowest from the highest measured value.

Parameters expected to vary over time were assessed for every season separately, parameters measured only once during the project

**Table 4**Univariable mixed negative binomial model of risk factors potentially associated with treatment incidence (TI<sub>UDD</sub>) in Swiss veal herds.

Parameter	Category	n <sup>i</sup>	Median	Quartile		Mean ± SD	Wald p-value
				25th	75th		
Agricultural zone <sup>l</sup>	Midland zone	13	8.1	1.6	30.9	15.5 ± 16.3	0.3
	Hill zone	6	6.5	2.5	27.3	12.6 ± 13.0	
	Mountain zone	24	7.5	3.6	11.7	9.6 ± 9.3	
Stocking method <sup>*,j</sup>	All-in all-out	12	25.4	6.8	34.6	22.7 ± 15.7	< 0.001
	Continuous	31	6.2	2.5	11.4	7.6 ± 7.4	
Access to outside pen <sup>*,j</sup>	Yes	25	8.7	3.8	19.9	13.3 ± 13.5	0.09
	No	18	6.0	2.0	13.6	9.7 ± 10.3	
Ventilation <sup>*,k</sup>	Natural	88	0.6	0	2.5	3.2 ± 6.5	< 0.001
	Mechanical	125	8.2	0.6	18.7	14.0 ± 17.8	
Shared airspace <sup>*,j,l</sup>	Yes	24	6.0	2.7	11.1	8.2 ± 8.0	0.08
	No	19	11.4	3.3	33.0	16.4 ± 15.1	
Hay or straw storage near calf pen(s) <sup>j</sup>	Yes	5	3.4	1.9	27.3	12.3 ± 21.2	0.89
	No	38	8.6	4.0	15.0	11.7 ± 11.0	
Pen change during fattening period <sup>l</sup>	Yes	22	7.4	4.0	11.5	8.2 ± 6.9	0.20
	No	21	9.8	2.1	30.2	15.6 ± 15.4	
Disinfection of calf pens <sup>*,j</sup>	≥ 3x per year	9	32.2	9.8	34.5	24.1 ± 13.1	< 0.001
	< 3x per year	5	4.4	3.7	9.1	6.0 ± 2.8	
	Never	29	6.2	1.7	12.1	9.0 ± 10.6	
Duration of sanitary break between groups <sup>*,j</sup>	≥ 1 week	8	3.2	1.2	12.6	6.9 ± 8.7	< 0.001
	< 1 week	7	34.4	25.7	35.2	31.9 ± 12.2	
	None	28	6.4	3.3	11.5	8.2 ± 7.5	
Cleaning of automatic feeder <sup>j</sup>	Daily	33	8.7	3.4	20.7	13.1 ± 13.1	0.20
	Less than daily	9	4.7	1.7	13.8	7.8 ± 8.3	
Hygiene of the feeder <sup>k</sup>	Good	126	2.2	0	12.7	9.2 ± 16.1	0.20
	Not good	81	3.8	0.3	14.5	10.4 ± 14.2	
Calves per drinking nipple <sup>*,k</sup>	1-5	29	0.1	0	2.5	2.5 ± 4.9	< 0.001
	6-10	96	1.4	0	7.5	5.0 ± 7.7	
	> 10	80	12.1	1.2	25.9	17.4 ± 20.3	
Vaccination against BRD <sup>*,e,k</sup>	Yes	82	7.5	1.4	19.9	15.2 ± 19.7	< 0.001
	No	131	1.0	0	9.2	6.0 ± 10.0	
Purchase <sup>*,j</sup>	Yes	34	9.5	4.3	18.1	13.5 ± 12.6	< 0.001
	No	9	2.5	0.4	5.7	5.4 ± 8.6	
Examination at arrival <sup>*,j</sup>	Yes	6	29.1	4.2	34.5	22.3 ± 15.3	0.002
	No	28	9.1	4.3	12.8	11.6 ± 11.4	
	N/A <sup>b</sup>	9	2.5	0.4	5.7	5.4 ± 8.6	
Quarantine upon arrival <sup>*,j</sup>	Yes	8	7.2	4.5	9.6	7.0 ± 3.9	0.002
	No	26	11.5	4.1	27.3	15.5 ± 13.7	
	N/A <sup>b</sup>	9	2.5	0.4	5.7	5.4 ± 8.6	
Metaphylactic treatment upon arrival <sup>*,k</sup>	Yes	53	15.0	1.9	33.3	21.1 ± 20.2	< 0.001
	No	160	1.4	0	7.8	5.7 ± 10.7	
Passage(s) through markets <sup>l</sup>	Yes	18	15.2	7.9	33.4	19.9 ± 14.3	< 0.001
	No	24	4.6	1.6	9.2	5.9 ± 5.9	
Maximum ammonia value (ppm) <sup>*,k,m</sup>	≤ 10	185	1.9	0	13.0	9.3 ± 15.6	0.16
	> 10	25	8.8	0.5	15.9	10.7 ± 12.6	

\* Factors tested in the multivariable model ( $p < 0.2$ ).<sup>b</sup> N/A: not applicable (no calf purchase).<sup>c</sup> BRD: bovine respiratory disease, vaccination with a modified live viral vaccine.<sup>i</sup> The total number of observations is not always the same because varying observations were recorded in every season and constant factors were recorded only at the beginning of the project.<sup>j</sup> Parameters measured/assessed once (overall).<sup>k</sup> Parameters measured/assessed seasonally.<sup>l</sup> Shared airspace with any cattle other than fattening calves.<sup>m</sup> In the calf pens per season.

period were called “overall”. As in previous studies (Bleul, 2011; Renaud et al., 2017), the months of June to August were defined as summer, September to November as fall, December to February as winter, and March to May as spring. Calves on the participating farms were assigned to the season during which they died or were slaughtered, to ensure that every calf was counted only once for the calculations.

### 2.3. Calf transport

When possible a member of the study team accompanied one transport per farm from the birth farm(s) to the fattening unit. Details about transport were recorded, including the birth farms of the calves, total number of transported calves, number of study calves among them, total number of stops during transport, number of stops on farms



and markets, distance in km and transport duration.

For all other (non-accompanied) calf transports, information including the date, birth farms of the calves, distance in km, transport duration, number of transported study calves, number of stops during the transport, and number of stops on markets was obtained by the farmer from the transporter immediately after the transport and recorded by use of a standardized form.

$$TI_{UDD} = \frac{\text{total amount of drug administered (mg)}}{UDD \text{ (mg/kg)} \times \text{number of calf days at risk} \times \text{standard weight (kg)}} \times 365$$

$$TI_{DDD} = \frac{\text{total amount of drug administered (mg)}}{DDD \text{ (mg/kg)} \times \text{number of calf days at risk} \times \text{standard weight (kg)}} \times 365$$

#### 2.4. Animal data, mortality rate and ADG

Dates of birth, purchase and slaughter, and breed of individual calves were extracted from the Swiss national animal movement database (Tierverkehrsdatenbank) after written informed consent for access was obtained from the farmers.

Mortality rate (in %) was calculated by dividing the number of dead calves by the total number of calves assigned to the season when death occurred, times 100. For determination of the ADG, an average weight of 72.1 kg at the beginning of the fattening period was assumed, as described in a previous study (Bähler et al., 2012). Individual animal weight was calculated from the carcass weight (available from slaughterhouse documents obtained from the farmers) divided by 0.56 (Bähler et al., 2012; Lava et al., 2016b). Weight gain during the fattening period was then divided by the duration of the fattening period to obtain the individual ADG. The mean ADG for each farm and season was calculated by dividing the sum of all individual daily weight gains by the number of calves slaughtered during that season. The duration of the fattening period was the number of days between calf purchase and slaughtering. For non-purchased calves (born on the fattening farm), the average duration of the fattening period of purchased calves on the farm was adopted. For farms fattening only non-purchased calves, the average age at purchase of all purchased calves participating in the study was used as the starting day for calculation of the duration of the fattening period.

All factors were calculated for every season separately. Overall measures for the entire study period were obtained from the means of the seasonal values.

#### 2.5. Data on treatment records and antimicrobial use

All data on antimicrobials from the treatment journals were entered in a spreadsheet (Excel 2010, Microsoft®, Redmond, WA, USA). To verify data quality, the information from the treatment journals was compared with the veterinarians' bills if available and, if diverging, the farmers were contacted for clarification. Both group treatments and individual treatments were registered and the route of administration (parenteral or oral) was recorded. The analysis of antimicrobial use was performed for every season separately as daily doses per animal per year.

Antimicrobial drug use was quantified based on two methodologies: TI was calculated with the used daily dose (UDD) and as the defined daily dose (DDD), whereby TI is the number of used daily doses and defined daily doses, respectively, of antimicrobial drugs per animal and year on the corresponding farm (Timmerman et al., 2006; Pardon et al., 2012a; van Rennings et al., 2013; Lava et al., 2016b).

The value UDD describes the effective daily treatment dose applied based on treatment records and DDD is defined as the assumed average dose of a drug per kg animal per day (EMA, 2014, 2016). The standard live weight of the calves at the time of treatment was set at 80 kg as

recommended by the European Medicines Agency (EMA, 2013). The number of days at risk was calculated as the number of calves assigned to the corresponding season multiplied by season duration in days. Yearly TI values were calculated by adding the TI values of the seasons of observation.

TI values  $TI_{UDD}$  and  $TI_{DDD}$  were calculated with the following formulas:

#### 2.6. Statistical analyses

The descriptive statistical analysis was performed with the software NCSS 10 (Kaysville, Utah, USA). Whether the continuous variables were normally distributed was explored by normal probability plots and the Shapiro-Wilk W test. The outcome ADG was normally distributed. Mortality and  $TI_{UDD}$  were not normally distributed because they represented an incidence. For descriptive statistics, frequency tables were generated for categorical variables. Median, interquartile range (IQR) and range, or mean, standard deviation (SD) and 95% confidence intervals (CI) were used to describe continuous variables.

A risk factor analysis was performed for the outcomes mortality, ADG, and  $TI_{UDD}$ . Because mortality and  $TI_{UDD}$  were not available at the level of the individual animal, the unit of analysis was the season. For the outcomes mortality and  $TI_{UDD}$ , the effects of 30 potential risk factors or confounders were tested. Categorical factors are shown in Tables 2 and 3. In addition, the following continuous factors were tested seasonally or overall per farm: percentage of dairy breed calves (overall), number of fattened calves per year (overall), average number of calves per pen (overall), bedded area (m<sup>2</sup>) per calf (seasonal), average transport distance (km; overall), average number of birth farms per 10 purchased calves (overall), average temperature (°C) and humidity (%) in the calf pens (seasonal), maximum variation of temperature and humidity during 72 h (seasonal), and maximum carbon dioxide concentration measured in the calf pens (seasonal). In seasonally evaluated factors, when the farms were visited more than once per season, the mean value of all measurements per season was used for the analyses.

For the outcome ADG, the effects of 29 factors, partially differing from the factors for mortality and  $TI_{UDD}$ , were tested. Categorical factors are presented in Table 4. In addition, the following continuous factors were tested seasonally or overall: percentage of dairy breed calves (overall), percentage of female calves (overall), number of fattened calves per year (overall), average number of calves per pen (overall), bedded area (m<sup>2</sup>) per calf (seasonal), percentage of purchased calves (seasonal), average temperature (°C) and humidity (%) in the calf pens (seasonal), maximum variation of temperature and humidity during 72 h (seasonal), and maximum carbon dioxide concentration in the calf pens (seasonal).

Correlation between potential risk factors was tested with Spearman or Pearson-Rank correlation coefficients for continuous variables and Phi coefficient for categorical variables. If correlation coefficients were > 0.7, only the biologically more meaningful factor was used for further analysis.

Multivariable analysis was performed with SAS 9.4 (SAS Institute Inc., Cary, USA), the unit of analysis was the fattening group (season). For mortality, neither a poisson nor a negative binomial model (with and without zero-inflation) resulted in a reasonable model fit. The outcome was therefore dichotomized into ≤3% mortality and >3% mortality, and analyzed with logistic regression. Mixed negative binomial and logistic models were created with SAS Proc GLIMMIX. For the

**Table 5**

Results of the multivariable mixed effects logistic regression model for mortality > 3%, the multivariable mixed negative binomial regression model for treatment incidence (TI<sub>UDD</sub>), and the multivariable mixed linear regression model for average daily weight gain in Swiss veal herds.

Outcome	Factors	Categories	Odds Ratio	95% CI <sup>a</sup>		Wald p-value
				lower	upper	
Mortality > 3%	Number of fattened calves per year (per 10 calves more)		0.92	0.92	0.93	< 0.001
	Hygiene of the feeder	Not good	Reference	–	–	–
		Good	2.26	1.09	4.68	0.03
Outcome	Factors	Categories	Effect size	95% CI <sup>a</sup>		Wald p-value
				lower	upper	
Average daily gain	Purchase	No	Reference	–	–	–
		Yes	–0.24	–0.35	–0.13	< 0.001
TI <sub>UDD</sub>	Quarantine upon arrival	Yes	Reference	–	–	–
		No	1.18	0.67	1.68	< 0.001
		N/A <sup>b</sup>	0.76	0.004	1.52	0.05
	Access to outside pen	No	Reference	–	–	–
		Yes	0.46	0.05	0.86	0.03
	Calves per drinking nipple	> 10	Reference	–	–	–
		6–10	–0.55	–0.96	–0.14	0.009
		1–5	–0.83	–1.58	–0.08	0.03
	Ventilation	Natural	Reference	–	–	–
		Mechanical	0.94	0.44	1.44	< 0.001
	Vaccination against BRD <sup>c</sup>	No	Reference	–	–	–
		Yes	0.97	0.57	1.37	< 0.001
	Maximum ammonia concentration (ppm) <sup>g</sup>	> 10	Reference	–	–	–
		≤ 10	–0.79	–1.36	–0.21	0.007

<sup>b</sup> N/A: not applicable (no calf purchase).

<sup>c</sup> BRD: bovine respiratory disease, vaccination with a modified live viral vaccine.

<sup>g</sup> Measured punctually during each farm visit.

<sup>a</sup> CI = Confidence interval.

outcome ADG, a mixed linear regression model was generated with SAS Proc MIXED. For the outcome TI<sub>UDD</sub>, a negative binomial regression model fitted best. Clustering of data at the farm level was accounted for by including the farm as a random effect in all models. As a first step, all risk factors were analyzed descriptively. Based on biologic plausibility, sufficient variability among farms and number of missing values, candidate variables for each model were identified. These variables were submitted to univariable screening. Only variables with a p-value < 0.2 in the univariable screening were entered into the multivariable model. Season was forced into all models as a fixed effect, because it had been an important factor in other studies (Busato et al., 1997; Assié et al., 2004; Bleul, 2011; Brscic et al., 2012; Fertner et al., 2016). For models with a small number of potential risk factors, the variable selection strategy was stepwise backward selection. If the number of variables in the initial model was too large, stepwise forward selection was used instead. Therefore, the final models for the outcomes mortality and TI<sub>UDD</sub> were built by a stepwise forward selection procedure, whereby only significant factors ( $p < 0.05$ ) or confounders that changed other regression coefficients by more than 20% were kept in the model. For the outcome ADG, non-significant variables ( $p > 0.05$ ) were excluded in a stepwise backward selection procedure, unless they changed other regression coefficients by more than 20%. Model fit for all models was assessed by Akaike's Information Criterion, visual assessment of residuals, and Shapiro Wilk W test on residuals for the linear model.

Transport factors (number of birth farms per 10 purchased calves, transport distance, passage(s) through market(s)) and factors of the continuous climate measurements (maximum variation of temperature and humidity) were only investigated in the univariable models because including them in the multivariable analysis would have led to

many missing values, as 9 farms did not purchase calves and continuous measures were only performed in two seasons (summer and winter).

### 3. Results

#### 3.1. Farms and farm data

From 56 farmers that initially showed interest in participating in the study, 12 were excluded because they fattened beef instead of veal calves ( $n = 7$ ), did fatten calves only in late fall, winter and early spring ( $n = 2$ ), fattened < 25 calves per year ( $n = 2$ ), or did not want to provide the necessary information ( $n = 1$ ). In addition, one farmer decided to quit the project after one visit. Thus, 43 farms participated in the study, of which 9 farms fattened only calves born on the farm and 34 farms purchased additional calves for fattening. A total of 4014 calves were fattened in the participating farms during the project.

Data from a total of 6 seasons were collected over all participating farms. Data for summer 2016 originate from 30 farms, for fall 2016 from 42 farms, for winter 2016/2017, spring 2017 and summer 2017 from all 43 farms, and for fall 2017 from 12 farms. The farms were under observation  $358 \pm 22$  days on average, with a maximum of 400 and a minimum of 317 days.

The most important features of the participating farms are described in Table 1.

#### 3.2. Mortality

The overall mortality during the project period was 5.1% (203/4014 calves). The mean overall mortality was 6.2% in large farms and



3.1% in small farms. On farm level, the mean mortality was  $3.7 \pm 3.6\%$ , with a minimum of 0 and a maximum of 15.6% (mean  $\pm$  SD,  $5.2 \pm 3.3\%$ ; range, 0–9.3% in large farms;  $3.2 \pm 3.6\%$  and 0–15.6% in small farms, respectively). Of all farms, 72% ( $n = 31$ ) had at least one dead calf during the project period.

### 3.3. ADG

The overall mean ADG of the calves included in the study was  $1.40 \pm 0.16$  kg (range, 1.00–1.92 kg). It was  $1.35 \pm 0.07$  kg (range, 1.27–1.45 kg) in large farms and  $1.41 \pm 0.19$  kg (range, 1.00–1.92 kg) in small farms.

### 3.4. Antimicrobial use

A total of 7060 treatments were recorded and used for the calculation of TI (Table 1). An indication for antimicrobial drug treatment was recorded for 5160 treatments (69%). The main indication was BRD (81.1%). Other indications were diarrhea (8.2%), otitis (4.9%), umbilical infection (0.7%), arthritis (0.1%), and others (5%). The majority of treatments were administered as group treatments (79%), whereas about 20% were individual treatments; 70% of the treatments were administered orally and 30% parenterally. The mean duration of the fattening period was  $116.4 \pm 14.2$  days, which corresponds to 3.1 fattening periods per year. Thus, the single calf was under treatment during a median of 2.6 days of its life. Performing this calculation with the  $TI_{DD}$  method resulted in 2.9 treatment days in a calf's life.

### 3.5. Risk factors for mortality

Descriptive statistics of potential categorical risk factors for mortality  $> 3\%$  and results of the univariable analysis are presented in Table 2. Furthermore, the following continuous factors were associated ( $p < 0.2$ ) with mortality  $> 3\%$ : dairy-breed calves (%), number of fattened calves per year, average number of calves per pen, bedded area ( $m^2$ ) per calf, maximum carbon dioxide concentration (ppm) in the calf pens, and maximum variation of temperature ( $^{\circ}C$ ) during 72 h.

Transport factors and factors of the continuous climate measurements were only investigated in the univariable models. The odds for mortality  $> 3\%$  was higher in farms with higher temperature variations (OR = 1.2 per  $^{\circ}C$ ; 95% CI: 1.0–1.4;  $p = 0.04$ ).

The results of the multivariable analysis are given in Table 5. The season of observation had a significant effect on mortality ( $p = 0.02$ ). In the multivariable model, mortality was highest in spring 2017 (mean  $4.45 \pm 7.0\%$ ), followed by winter 16/17 (mean  $4.42 \pm 6.6\%$ ), summer 2017 (mean  $3.98 \pm 6.7\%$ ), fall 2016 (mean  $2.66 \pm 5.2\%$ ), fall 2017 (mean  $2.0 \pm 3.4\%$ ) and summer 2016 (mean  $0.66 \pm 2.1\%$ ).

### 3.6. Factors associated with ADG

Descriptive statistics of potential categorical risk factors for decreased ADG and results of the univariable analysis are presented in Table 3. In addition, the following continuous factors were associated with ADG ( $p < 0.2$ ): dairy breed calves (%), female calves (%), bedded area ( $m^2$ ) per calf, purchased calves (%) and maximum carbon dioxide concentration in the calf pens.

The results of the multivariable analysis are given in Table 5. In addition, in the multivariable model, a significant association with the season of observation was present ( $p < 0.04$ ). The ADG was highest in fall 2017 (mean  $1.45 \pm 0.2$  kg), followed by fall 2016 (mean  $1.44 \pm 0.3$  kg), spring 2017 (mean  $1.42 \pm 0.2$  kg), summer 2017 (mean  $1.40 \pm 0.2$  kg), summer 2016 (mean  $1.39 \pm 0.2$  kg) and winter 16/17 (mean  $1.36 \pm 0.2$  kg).

### 3.7. Risk factors for increased antimicrobial use

Descriptive statistics of potential categorical risk factors for increased antimicrobial use and results of the univariable analysis are presented in Table 4. Furthermore, the following continuous factors were associated ( $p < 0.2$ ) with  $TI_{UDD}$ : number of fattened calves per year, average number of calves per pen, bedded area ( $m^2$ ) per calf, transport distance (km), average number of birth farms per 10 purchased calves, average temperature ( $^{\circ}C$ ) and humidity (%) in the calf pens, and maximum carbon dioxide concentration in the calf pens.

Transport factors and factors of the continuous climate measurements were only investigated in the univariable models. The  $TI_{UDD}$  value was higher in farms which purchased calves having gone through markets (effect size = 1.3;  $p < 0.001$ ) and in farms with higher numbers of birth farms (effect size = 0.17 per additional birth farm per 10 purchased calves;  $p = 0.004$ ).

The results of the multivariable analysis are given in Table 5. A significant association with the season of observation was also present ( $p < 0.001$ ). In the multivariable model, treatment incidence was highest in winter 2016/2017 (mean  $14.0 \pm 19.5$  days / calf / year), followed by spring 2017 (mean  $11.45 \pm 19.1$  days / calf / year), fall 2016 (mean  $11.19 \pm 11.4$  days / calf / year), summer 2017 (mean  $6.72 \pm 11.8$  days / calf / year), summer 2016 (mean  $4.50 \pm 10.7$  days / calf / year) and fall 2017 (mean  $3.48 \pm 6.2$  day / calf / year).

## 4. Discussion

Significantly associated risk factors in the management of Swiss veal farms were found for the three main outcomes of the study, mortality, daily weight gain and treatment intensity.

The overall mortality rate was 5.1% (6.2% in large herds and 3.1% in small ones). This value is relatively high in comparison with previous Swiss studies where mortality rates of 3% (Luginbühl et al., 2012), 3.6% (Bähler et al., 2012) and 4.1% (Lava et al., 2016b), respectively, were reported. The significantly decreased risk of mortality  $> 3\%$  observed in association with increasing numbers of calves fattened per year in the multivariable analysis is not easily understandable, particularly given that the outcome in the univariable analysis was in the opposite direction, and mortality in large farms was significantly higher (6.2%) than in small farms (3.1%). Furthermore, this finding is in contradiction with the findings of previous studies where increased numbers of calves and larger calf groups were associated with higher mortality (Svensson et al., 2006; Woolums et al., 2013; Lava et al., 2016a, 2016b). A possible explanation for the present findings may be that a single dead calf can already lead to a mortality rate of  $> 3\%$  in small farms, whereas a larger number of dead calves is necessary to reach a corresponding mortality rate in large farms. Thus, the fact that many of the participating farms only fattened a small number of calves was not optimal for the assessment of risk factors for mortality  $> 3\%$ , because the death of a single calf was often sufficient to reach a mortality of  $> 3\%$ . Participation of more large farms would have minimized the effect of the single calf's death on mortality rates, however the participation of more large farms would not have reflected the actual situation in Switzerland, as small farms are by far more common than large ones (Lava et al., 2016a).

The association of a higher maximum variation of temperature (difference between the highest and the lowest temperature measured over 3 measurement days) with mortality  $> 3\%$  in the univariable model was not surprising, as Martin et al. (1975) had also observed an association of large variations of temperature with increased mortality. Others also reported that large temperature variations lead to thermic stress in calves (Roland et al., 2016).

The positive association of a good hygiene of the feeder with mortality  $> 3\%$  in the multivariable model may be due to reverse causality, as farmers having more severe problems are more likely to have already undertaken attempts to counteract them, e.g. with better hygiene.

The overall mean ADG was  $1.40 \pm 0.16$  kg. In other studies the mean ADG ranged from 0.95 to 1.7 kg (Wilson et al., 2000; Thompson et al., 2006; Windeyer et al., 2014). Calf purchase was significantly associated with decreased ADG. This finding is in accordance with the results of another study in which a lower ADG was observed in transported calves as compared to non-transported control calves (Adams-Progar et al., 2015). Purchase has also been shown to be a risk factor for increased TI (Martin et al., 1982; Fertner et al., 2016; Lava et al., 2016a). In addition, a significantly lower carcass weight or ADG during the feeding period was found for diseased and treated calves in comparison with healthy calves in several studies (Bateman et al., 1990; Vortal et al., 1996; Gardner et al., 1999; Thompson et al., 2006; Pardon et al., 2013). These findings suggest that the negative association of purchase with ADG is caused by negative effects of purchase on calf health. Feed composition may also influence ADG, however a detailed feed analysis in the participating farms was beyond the scope of our study.

Regarding TI, the finding of a higher  $TI_{UDD}$  in mechanically ventilated barns is consistent with another study in which respiratory disorders were more frequent in mechanically ventilated barns. The authors suggested that the reason for increased BRD incidence was exposure to drafts (Brscic et al., 2012). It is generally recognized that calves are very susceptible to drafts, thus this assumption may also be valid for the present study. Lundborg et al. (2005) reported a significant association between drafts and increased respiratory sounds in calves. Lava et al. (2016a) found access to an outside pen to be a significant risk factor for mortality  $\geq 3\%$  and indicated exposure to drafts as the most probable reason for this observation. The variation of temperature and humidity may also be greater in stables with access to an outside pen than in closed stables, which would corroborate the observation that manual temperature control resulted in increased BRD risk in comparison to automatically adjusted temperature control (Windeyer et al., 2014).

The association of an ammonia level  $> 10$  ppm, the recommended upper level in Swiss barns (BLV, 2009), with increased  $TI_{UDD}$  was not surprising, as the concentration of ammonia gases has an influence on calves' vulnerability to BRD (Assié et al., 2009). It has been shown in swine that an ammonia concentration of 5 ppm or more led to increased *P. multocida*-induced turbinate atrophy (Hamilton et al., 1996). This suggests that a negative impact of ammonia regarding the development of BRD is already present at low ammonia concentrations.

The fact that a higher number of calves per drinking nipple was associated with increased  $TI_{UDD}$  may be due to the high probability that farms with more calves per drinking nipple fatten more calves per year and, therefore, have larger calf groups. Higher numbers of antimicrobial treatments in larger farms or calf groups have been observed previously (Luginbühl et al., 2012; Lava et al., 2016a, 2016b).

The association of vaccination against BRD with increased TI was surprising, although increased mortality and increased health costs in vaccinated cattle groups compared to non-vaccinated ones have been reported by others (Martin et al., 1982). These authors suggested that not vaccination in itself, but the handling stress may be responsible for the negative effect of vaccination. Furthermore, this finding may also be explained by reverse causality, as farmers with more animals suffering from respiratory diseases tend to vaccinate more often (Assié et al., 2009). Another possible contributing factor may be interference of maternal antibodies with the vaccine response. Reduced antibody production after vaccination due to the presence of maternal antibodies has been reported, leading to reduced protection against infectious diseases. Immunization is only successful when maternal antibodies have already declined, but this point in time depends on many factors and is, therefore, not easily predictable (Niewiesk, 2014). In our study, the questionnaire only addressed whether the calves were vaccinated on arrival at the fattening unit. The study calves were mostly immunized with an attenuated live vaccine against BRSV and PI3

(Risposval<sup>®</sup>RS + PI3 IntraNasal, Zoetis, Zürich). According to the manufacturer's information, vaccination is possible from an age of one week. Protection against viral infections starts after 5–10 days and should last approximately 12 weeks. Therefore, if calves are vaccinated only upon arrival in the fattening unit, they remain unprotected for the following 5–10 days. Vaccination would thus work more effectively if it was administered on the birth farm in order to provide time for its effect to unfold until the calves are transported to the fattening unit. However, under the present Swiss farming conditions, farmers on the birth farms see no added value in vaccination and are consequently reluctant to spend money on vaccines. Solving this problem would require a better cooperation between fattening units and birth farms.

The factors associated with  $TI_{UDD}$  identified in the univariable analysis are in accordance with the results of previous studies (Autio et al., 2007; Sanderson et al., 2008; Fertner et al., 2016; Lava et al., 2016a).

The single calf was under treatment during 3.8 days of its life on average (median 2.6). Performing this calculation with the  $TI_{DDD}$  method resulted in 4.0 treatment days in a calf's life (median 2.9). Both  $TI_{UDD}$  and  $TI_{DDD}$  values are distinctly lower than in a recent Swiss study where an overall mean TI of 21 days per calf and year was found, which corresponds to 7 treatment days per calf on average (Lava et al., 2016b). In addition, those authors calculated TI according to the  $TI_{ADD}$  method, with a standard weight of 164 kg, which generally leads to an underestimation of TI. Current recommendations prescribe to calculate  $TI_{UDD}$  and  $TI_{DDD}$  with a standard weight of 80 kg (EMA, 2013), as in the present study. Thus, the difference in observed treatment intensity between the two studies would be even greater by a factor 2 if the difference in standard weight is taken into account. One possible explanation for this discrepancy is the fact that antimicrobial use in Switzerland has been decreasing continuously since 2008 (BLV, 2017). On the other hand, long-acting factors are not used for the calculation of  $TI_{DDD}$  because the European Medicines Agency (EMA) suggests assigning the same DDD to any one substance independently of whether it is formulated as a long acting product or not, as the impact of long-acting injectables is considered to be minor (EMA, 2014). Accordingly, no long-acting factor was used for the calculation of  $TI_{UDD}$ , which can lead to an underestimation of TI. This assertion is supported by the fact that the overall  $TI_{DDD}$  was higher than the overall  $TI_{UDD}$ . It has been described in many cases that the UDD can deviate from the DDD or ADD, respectively (Callens et al., 2012; Pardon et al., 2012a; Persoons et al., 2012; Merle et al., 2014; Collineau et al., 2017).

The  $TI_{UDD}$  and  $TI_{DDD}$  values were massively higher in large farms than in small farms (median = 5, IQR = 2.1–9.6, vs. median = 26, IQR = 14.7–34.4 for  $TI_{UDD}$ , and median = 7, IQR = 2.4–12.2 vs. median = 18, IQR = 13.6–31.6 for  $TI_{DDD}$  in small vs. large farms, respectively). This may be caused at least in part by the fact that a greater percentage of calves were treated metaphylactically upon arrival in large farms in comparison with small farms (in 73% of large farms vs. 9% of small farms). In addition, entire calf groups were mostly treated in large farms, whereas more often individual sick calves were treated in small farms (large farms: 87% group treatments vs. 13% individual treatments; small farms: 48% group treatments vs. 52% individual treatments).

The main indication for antimicrobial treatment was BRD (81.1% in the present study), in accordance with the results of other studies (Pardon et al., 2012a; Fertner et al., 2016; Lava et al., 2016b). This confirms that preventive measures targeted at the reduction of respiratory infections should have an important impact on antimicrobial use in veal calf operations.

In the present study, a significant seasonal influence was observed on TI, mortality and ADG. However, the number of study farms was not the same in every season, ranging from 12 to 43 farms. Therefore, the significance of these results is difficult to evaluate. However, TI was highest in winter, as compared to other seasons, which is in accordance

with the results of other studies (Busato et al., 1997; Svensson et al., 2003; Assié et al., 2004; Bleul, 2011; Brscic et al., 2012; Windeyer et al., 2014; Fertner et al., 2016).

It is well known that factors not only in the fattening unit but also on the birth farm influence calf health, e.g. colostrum management (Virtala et al., 1999). The evaluation of factors in the birth farms that may have a significant effect on the later calf health status was beyond the scope of our study, but it would be beneficial to investigate the influence of factors in the birth farms on veal calf health in future studies.

Participation in this study was voluntary after recruitment through information in agricultural publications. It is possible that the farmers' motivation to participate was increased when either the farm was running well or the farmer was having problems with the calves and hoped for solutions through participation in the study. Therefore, the method of acquisition of participating farms may have resulted in a selection bias. Due to practical limitations, only a limited number of farms could be included in the study. Therefore, the power of the study was only sufficient to detect associations with a relatively large effect on TI<sub>UDD</sub>. Also, risk factors that were significant in the univariable analysis only should be interpreted with caution, because the large number of factors tested in the screening might have caused some falsely significant results (type I error). Finally, the results of this study may not be generalizable to other countries, as the Swiss veal fattening system differs from the practice used in EU-countries (Sans et al., 2009).

## 5. Conclusions

Based on the identified risk factors for mortality > 3%, decreased ADG and increased TI, targeted recommendations for veal calf management and housing can be given. Calf purchase should be minimized as far as possible and passage(s) of calves through markets avoided. The calves should be examined and quarantined upon arrival in the fattening farm, sick animals should be sent back or treated immediately as needed. Ideally, purchased calves should be vaccinated against BRD already on the birth farm. The number of calves fattened should be kept at a manageable level and the calves should be reared in small groups of a maximum of ten animals. Contact between groups should be prevented. Specific attention should be paid to ventilation in order to ensure good air quality without producing drafts, and calf pens should be regularly cleaned to ensure that ammonia concentrations remain low. Sick calves should be separated to avoid the spread of disease and treated appropriately as soon as possible. These efforts should allow for improved calf health and, in consequence, for reduced antimicrobial use, thereby minimizing the impact of the veal fattening sector on the selection of resistant bacteria.

## Conflict of interest

The authors declare no conflict of interest.

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